REMARKS

1. Status of claims

After entry of the above amendment, claims 1-23 and 102 are pending.

2. Support for amendment

The above amendment clarifies various terms recited by the claims. No new matter has been added.

3. Claim rejections under 35 U.S.C. §112

The Examiner rejected claims 1-23 and 102 under 35 U.S.C. §112, second paragraph, for allegedly failing to distinctly claim the invention. Specifically, claim 1 allegedly lacked clarity for reciting "when cultured in a culture medium." By the above amendment, this phrase has been deleted from claim 1. It is clear from context that the recited yeast strain produces essentially no ethanol during the aerobic culturing step of claim 1. Also, the Examiner alleged the phrase "essentially no ethanol" in claim 1 was unclear. The skilled artisan will understand this phrase to mean ethanol is undetectable, i.e., it is only present at levels below the detection limit, which levels include zero ppm. In addition, the Examiner pointed to the phrase "wherein a protein resulting from the expression" in claims 1 and 102 was unclear. By the above amendment, this phrase has been changed to "wherein a protein resulting from the expression of the exogenous lactate dehydrogenase gene…." Finally, the Examiner pointed to "essentially the same minimal medium" in claim 8 as lacking antecedent basis in claim 1. Claim 1 has been amended to recite the first culture medium is a minimal medium, and claim 8 has been amended to remove the word "essentially."

Second, the Examiner rejected claims 1-10, 12-20, 22-23, and 102 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to convey the inventors had possession of the claimed invention. The Examiner alleges the specification teaches the preparation of lactic acid using a few modified acid-tolerant (AT) yeast strains expressing a few exogenous lactate dehydrogenase (LDH) genes. He further alleges the specification does not teach the structures of all LDH genes, defining features of AT yeast strains, or the modification of all AT yeast strains with all LDH genes. Applicants traverse this rejection.

The written description requirement set forth in 35 U.S.C. §112, first paragraph implements the principle that a patent must describe the technology that is sought to be patented. The written description requirement also conveys that an applicant has invented the subject matter which he claims. In *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005), the United States Court of Appeals for the Federal Circuit addressed the written description requirement. The present specification, in light of the holdings in *Capon v. Eshhar*, complies with the written description requirement.

Concerning AT yeast strains, the specification, in light of the plain meaning of the words "acid tolerant," makes clear that yeast encompassed by this term are all strains capable of producing lactic acid in minimal medium at lower pHs than their parent strains (p. 4, lines 21-22). AT yeast have been prepared by modification of a parent strain (p. 4, lines 22-27). Although the claims are not so limited, certain AT yeast can produce lactic acid in a medium with a pH of 3.5 or less (p. 4, lines 28-30). This language clearly defines AT yeast strains and makes it clear to the skilled artisan that Applicants possessed the claimed invention. As held in *Capon v. Eshhar*, the written description requirement "does not state that every invention must

be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." 76 USPQ2d at 1085. Yeast have been known and used for thousands of years, and the science of yeast culture, including media and pH for yeast growth and production and non-recombinant genetic modification, has been studied for decades. Therefore, there is no need to describe every possible AT yeast strain that can be used in the present invention.

Concerning LDH genes, the specification points to the public availability of six LDH sequences, two from *Lactobacillus* bacteria, two from *Bacillus* bacteria, one from an animal (bovine), and one from a fungus (*Rhizopus oryzae*). (p. 6, lines 8-13). As the Court held in *Capon v. Eshhar*, there is no *per se* rule that a sequence listing must be presented for every biological sequence claimed in a patent application. 76 USPQ2d at 1084-1085. The above list represents examples of LDH genes, which, in light of the functional information contained in the phrase "lactate dehydrogenase," render clear to the skilled artisan that Applicants possessed the invention as claimed.

The preparation of AT yeast strains expressing exogenous LDH genes involves known biotechnology techniques that have been in common use for decades (p. 23, line 24 to p. 25, line 12). In light of *Capon v. Eshhar*, the written description is sufficient in light of the skilled artisan's knowledge of the art. For at least these reasons, Applicants submit this rejection of claims 1-10, 12-23, and 102 is improper and should be withdrawn.

The Examiner also rejected claims 1-10, 12-23, and 102 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement over their full scope. Specifically, he alleged that methods of producing lactic acid by the use of any AT yeast strain expressing any exogenous LDH gene were not enabled. Applicants traverse this rejection.

The Examiner alleges that the predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires more information than that provided by "few LDH genes." This allegation is incorrect. The specification points to six known LDH genes with known sequences, as discussed above, and these known sequences, along with knowledge of the desired LDH activity, provide sufficient information for the skilled artisan to identify other LDH genes from the same or other organisms or to modify LDH genes' nucleotide sequences in order to use the identified or modified genes in the present method. The skilled artisan can use well-known techniques and information, such as sequence alignments or the degeneracy of the genetic code, in doing so. Therefore, any experimentation required is not undue. For at least these reasons, Applicants submit this rejection of claims 1-9, 12-23, and 102 is improper and should be withdrawn.

4. Claim rejections under 35 U.S.C. §102

The Examiner rejected claims 1-10, 12-23, and 102 under 35 U.S.C. §102(b) as being anticipated by Hause et al., US 2003/0228671 ("Hause"). Specifically, the Examiner pointed to Hause as teaching the use of recombinant *Saccharomyces* or *Kluyveromyces* expressing exogenous LDH to produce lactic acid (95 g/100 g glucose) at pH 2.3 or less in a culture medium containing at least glucose and one nitrogen source, and also as teaching the use of such yeasts wherein no pyruvate was produced. Applicants traverse this rejection.

The only mention of use of *Saccharomyces* yeast by Hause is at paragraph 0067, which recites "Yeast cells that do not accumulate pyruvate, i.e., that naturally metabolize pyruvate to ethanol or other metabolization products, are preferred." This teaches away from present claims 1-10 and 12-23, which teach a method in which a yeast strain produces essentially no ethanol.

The only working examples given in Hause of lactic acid production (Examples 1K, 1L, 2F, 2G, 3E, and 3F) show lactic acid production by *Kluyveromyces marxianus*, and of these, only Examples 3E and 3F report a process wherein no ethanol was produced.

The teachings of Hause are also directed to the use of complex media, containing YPD, added glucose, and in Example 3E, calcium carbonate. YPD is a known medium generally containing 10 g/L yeast extract, 20 g/L peptone, and 20 g/L dextrose. Yeast extract and peptone are protein-rich materials of undefined composition. All the present claims recite the use of minimal media, which is defined at p. 19, lines 7-14, as excluding materials of undefined composition, specifically excluding by name yeast extract and peptone.

The teachings of Hause are also directed to the production of lactic acid during a microaerobic production phase. Microaerobic conditions are defined at paragraph 0079 and are distinguished from aerobic conditions, *ibid*. In contrast, the present claims are directed to lactic acid production involving aerobic culturing of yeast.

In addition, various dependent claims have further distinctions over Hause. Claims 2-4 and 13-16 recite the use of an AT yeast strain that is C2 carbon source independent, as defined at p. 17, lines 18-24. At p. 18, lines 20-23, Applicants make clear that yeast extract is a complex carbon source, i.e., one that is undefined and therefore may contain carbon sources containing two carbon atoms. As such, Hause's use of YPD implies that Hause's yeast are C2 carbon source dependent, which is in distinction to these claims.

Claim 10 recites the use of an AT yeast strain from species *Saccharomyces cerevisiae*. Hause does not teach acid tolerant *Saccharomyces* yeast at paragraph 0067.

For at least the foregoing reasons, it is clear Hause does not teach every element of any of claims 1-10, 12-23, and 102. Applicants submit this rejection of these claims is improper and request it be withdrawn.

5. Conclusion

Applicants submit all pending claims 1-23 and 102 are in condition for allowance. The Examiner is invited to contact the undersigned patent agent at (713) 934-4065 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

WILLIAMS, MORGAN & AMERSON, P.C.
CUSTOMER NO. 23720

November 29, 2006

/Raymund F. Eich/
Raymund F. Eich, Ph.D.
Reg. No. 42,508
10333 Richmond, Suite 1100
Houston, Texas 77042
(713) 934-4065
(713) 934-7011 (fax)

AGENT FOR APPLICANTS